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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,849	05/23/2001	Jerome O. Cantor	C35795/125237	1932

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EXAMINER
HENRY, MICHAEL C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 08/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,849	CANTOR ET AL.	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-33 and 37-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *31,32 and 41-47* is/are allowed.

6)☒ Claim(s) *33 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 04/28/06.

The amendment filed 04/28/06 affects the application, 09/853,849 as follows:

1. Upon further consideration applicants arguments filed 04/28/06 are convincing and consequently the rejection of the prior office action is withdrawn. Consequently, this office action is made non-final.

   The responsive to applicants' arguments is contained herein below.

Claims 31-33, 37-47 are pending in application

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "chemically modified", in claim 38, renders the claim indefinite. More specifically, it is unclear how said polysaccharide is chemically modified especially since there are mumerous ways in which said polysaccharides can be modified, based on the functional groups they contain or possess.

The abbreviation or term "DPPC/DPPG", in claim 40, renders the claim indefinite. More specifically, it is unclear what the abbreviation or term, DPPC/DPPG designates or means.

It should be noted that all claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation. Applicants are not enabled for the combinations of polysaccharide and a drug as claimed in claims 33 and 39.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claim 31 is drawn to a system for delivering a polysaccharide formulation to a respiratory tract of a mammal, comprising: a mixture comprising a polysaccharide having a molecular weight of between about 50,000 and 1.5 x 10^6 Daltons at a concentration of less than about 5.0 mg/ml (w/v) of polysaccharide, and a breathable fluorocarbon propellant; a canister adapted to contain said mixture under pressure; a valve connected to said canister for regulating delivery of said mixture; and a nozzle interconnected with said valve for transforming said mixture under pressure into an inhalable aerosol mist when said valve is actuated." Dependent claim 32 is drawn to said composition or system comprising the polysaccharide in the aerosol mist is of specific median mass distribution sizes. Claim 33 and 39 are drawn to said system or composition wherein the said mixture or solution further comprises a drug. Claims 34, 38, 40, 41, 42, 43, 45-47 are drawn to said system or composition wherein the polysaccharide is chemically modified, wherein the said system further comprises specific drugs, wherein the polysaccharides are specific polysaccharides and of specific molecular weights.

The state of the prior art

Recent advances in medicine have produced several alternative modes of drug delivery. Drugs which were previously only available in injectable forms, are now available in less invasive forms such as oral tablets or capsules, sustained release devices, and transdermal patches. Many of these advances, however, have occurred with protein based or small molecule drugs. Delivery of polysaccharides for therapeutic or prophylactic purposes is still associated with some problems. The pulmonary delivery of polysaccharides of both unformulated and formulated polysaccharides are known to be of limited success due to their poor penetration to

and resultant poor pharmacokinetics performance. Fluorocarbons are commonly used as propellants for aerosol formulations. For example, Green (WO 96/19968) discloses an aerosol formulation for administration by inhalation containing a fluorocarbon propellant, a medicament and a sugar (not a polysaccharide) including dextrose, sucrose and lactose, for treating respiratory disorders (see abstract). Also, a delivery system for localised administration of a medicament to the upper respiratory tract, comprising a medicament for treating the upper respiratory tract, an ionic polysaccharide and a crosslinking agent has been disclosed (US 5,912,007, see abstract and claims). Combination therapy, and drug-drug interactions are known in the art to have various effects, and when physicians use several drugs in combination, they face the problem of knowing whether a specific combination in a given patient has the potential to result in an interaction, and if so, how to take advantage of the interaction if it leads to improvement in therapy or how to avoid the consequences of an interaction if they are adverse. A potential drug interaction refers to the possibility that one drug may alter the intensity of the pharmacological effects of another drug if given concurrently. The net result may be enhanced or diminished effects of one or both of the drugs, or the appearance of new effects which is not seen with either drug alone. The frequency of significant beneficial or adverse effects is unknown. The interaction between the drugs may be pharmacokinetic, i.e. alteration of the absorption, distribution, or elimination of one drug by another, or may be pharmadynamic, i.e. interactions between agonists and antagonists at drug receptors. The most important drug-drug interactions occur with drugs that have serious toxicity and low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences. Additionally, drug-drug interactions can be clinically important if the disease being controlled with the drug is

serious or potentially fatal if left under treated. Drugs are known to interact at any point during their absorption, distribution, metabolism, or excretion; the result being an increase or decrease in concentration of the drug at the site of action. As individuals vary in their rates of disposition of an given drug, the magnitude of an interaction that alters pharmacokinetic parameters is not always predictable, but can be very significant. See Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 10th Edition, McGraw-Hill Medical Publishing Division, 2001, pages 54-56. Thus, the teachings of the book clearly support the fact that the instant claimed invention, which is drawn to a composition or system comprising a combination of any polysaccharide and any drug to be delivered to a respiratory tract of a host (e.g., a human) (as recited in claims 33 and 39), is highly unpredictable.

The level of predictability in the art

As seen by Goodman & Gilman, the art of combination therapy is unpredictable. Drug-drug interactions are known to be beneficial or adverse, yet there is no way to know until the drugs are actually tested in combination with each other. Consequently, the utility of applicant's combination comprising a polysaccharide and any drug is highly unpredictable in light of the foregoing disclosure that pertains to the unpredictability of drug-drug interactions.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and the examples provided in order to use the claimed composition commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the claims as written. More specifically, there is no data or examples that disclose the use or preparation of the polysaccharide and drug combination

that is being claimed. Furthermore, applicants have not provided any indication of what drugs might be toxic and what the drugs therapeutic indexes are. Applicants have merely listed various drugs in the specification.

The existence of working examples

There are no working examples in the instant application that disclose the use of a polysaccharide/drug combination. There are no formulations made that comprises said polysaccharide/drug combination, and said formulations have not been tested in any capacity on any subjects. Applicants state that "In one variation to this method, the solution further comprises a drug" and that the drug may be selected from the group consisting of some specifically recited drugs (see page 2 of the specification).

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable one to make or use the combination of the claimed polysaccharide and all drugs or any drug of choice without undue experimentation. It is noted that the specification should teach how to make and use the invention, not teach how to figure out for oneself how to make and use the invention. See ***In re Gardner, 166 USPQ 138 (CCPA 1970).***

Allowable subject Matter

The following is an examiner's statement of reasons for allowance: The examiner has found claims 31, 32, 41-47 to be unobvious over the prior art of record and therefore to be allowable over the prior art of record. The present invention relates to a composition comprising a polysaccharide of specific molecular weight and specific concentration together with a

breathable fluorocarbon propellant, whereas the composition of the prior art (US 5,633,003 and US 5,376,386) documents contains a polysaccharide of different molecular weight and concentration, and lacks the presence of the said breathable fluorocarbon propellant. Furthermore, these differences in the composition of the instant claims are not suggested, and are unobvious over the prior art documents.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry

7/28/06

Shaojia Anna Jiang, Ph.D.
Supervisory Patent Examiner
Art Unit 1623

July 26, 2006.